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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,481	01/08/2001	Mark Marchionni	47506 (47843)	4213

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EXAMINER	
GUCKER, STEPHEN	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 01/21/2004

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,481	MARCHIONNI ET AL.	
	Examiner	Art Unit	
	Stephen Gucker	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-82* is/are pending in the application.

4a) Of the above claim(s) *5-25,35-40 and 42-82* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☒ Claim(s) *26-34 and 41* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/18/02* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election of Group I, claims 1-4, 26-34, and 41 (in part - only drawn to methods of administering a polypeptide - the claims must be amended to reflect the restriction requirement) in Paper No. 20, filed 10/6/03, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 5-25, 35-40, and 42-82 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 20.

2. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was

unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

The Examiner notes that applicant's "Added Pages For Application Transmittal Where Benefit Of Prior U.S. Application(s) Claimed" form is unclear according to the boxes checked off. As such, the first sentence of the specification only contains reference to provisional U.S. application 60/091,791 because the specification was not amended. If applicant wishes to claim benefit to PCT/US99/15106, the first sentence of the specification should be amended to read as follows:

"This application is a continuation of PCT/US99/15106, filed July 2, 1999, which claims the benefit of U.S. provisional application number 60/091,791, filed July 6, 1998."

It should be noted by applicant that the instant application cannot directly claim the benefit of the provisional application because the instant application was filed over a year past the filing date of the provisional application.

3. Applicant's claim to foreign priority under 35 U.S.C. 119 is improper. A U.S. patent application cannot claim foreign priority to an international PCT application filed in the U.S. that names the U.S. as one of the participating countries because the U.S. is not a foreign country in this situation.

4. Claims 26-34 and 41 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend upon another multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims 26-34 and 41 have not been further treated on the merits.

5. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for these reason(s): Page 22 of the specification recites SEQ ID NO:3 (line 27) and SEQ ID NO:4 (line 28). These sequences do not appear in either the paper or CRF copy of the sequence listing. A new CRF and paper copy of the sequence listing are required that include SEQ ID NOs:3 and 4.

6. Applicant should review the instant Application in its entirety for compliance with the sequence rules, paying particular attention that all sequences recited throughout the disclosure in its entirety have SEQ ID NOs and that the SEQ ID NOs recited are found in both the CRF and paper copy of the Sequence Listing. Applicant must comply with the sequence rules and the remainder of the entire Office action simultaneously. Otherwise, the applicant will receive a Notice of Non-Responsive Reply.

7. Applicant is given the shortened statutory period of THREE MONTHS from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims recite methods of treatment using fragments or derivatives of GDF-1. However, no specific fragments or derivatives of GDF-1 that possess therapeutic efficacy are adequately described in the disclosure. The specification describes that a fragment must be at least 8 amino acids long, but there is absolutely no description in the specification as to which of the many 8 amino acid long or longer peptide fragments or derivatives of the 357 amino acid long full length GDF-1 protein would possess the biological function of the entire, unfragmented GDF-1 protein. There is no adequate description in the specification as to which specific amino acids in the GDF-1 sequence can be deleted, added to, or substituted to the GDF-1 amino acid sequence and still retain its biological function. No critical domains or regions of the GDF-1 protein are described that bestow upon the molecule as a whole or in part its therapeutic efficacy. Because of the unpredictable nature of predicting function from structure that is well-known in the protein/polypeptide arts (see Rudinger), no fragment or derivative of GDF-1 that possesses therapeutic efficacy is adequately described such that one skilled in the art would recognize that the disclosure describes

a biologically active fragment or derivative because no specific fragments or derivatives are disclosed that possess biological function and the two working examples (Examples 4 and 5) only describe the use of the entire GDF-1 protein. Removing the fragment or derivative language from the claims and by reciting "(SEQ ID NO:2)" after GDF-1 is recited in the claims would obviate the grounds of this rejection.

9. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods using GDF-1 (SEQ ID NO:2) in conjunction with NT-3, or using GDF-1 (SEQ ID NO:2) alone on cerebellar granule cells, to promote neuronal fiber outgrowth or neuronal survival, does not reasonably provide enablement for methods of preventing or treating nerve cell death or degeneration at all, or methods using GDF-1 without NT-3 or using GDF-1 alone, except on cerebellar granule cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The specification teaches that GDF-1 was ineffective on chick sympathetic ganglion explants not exposed to NT-3 (page 25, lines 28-29 and Table 1). Chicken sympathetic ganglion contain multiple neuronal cell types, and the absence of any effect of GDF-1 by itself on these multiple neuronal cell types is direct experimental evidence that the prophetic disclosure is not commensurate with the broad scope of the claims which encompass treating or preventing nerve cell death or degeneration from a variety of conditions (claim 2) or after injury (claims 3-4). Treating or preventing nerve cell *death* would encompass bringing dead neurons back to life or rendering them immortal, and such is clearly not enabled by this or any other disclosure.

No working examples are provided that enable the use of GDF-1 alone, except on a single specific neuronal cell type, cerebellar granule cells, which are phenotypically uniform, unlike the mixtures of cells that are in a chicken sympathetic ganglion. The grounds of this rejection could be obviated by amending the claims to recite a method of promoting neuronal fiber outgrowth or neuronal survival by administering a therapeutically effective amount of both GDF-1 (SEQ ID NO:2) and NT-3, or, a method of promoting neuronal fiber outgrowth or neuronal survival of cerebellar granule cells by administering a therapeutically effective amount of GDF-1 (SEQ ID NO:2) to a patient in need of neuronal fiber outgrowth or neuronal survival of cerebellar granule cells. The applicant should note that attempts to incorporate sequence identity, hybridization language, fragments, derivatives, etc. into the claims may necessitate further U.S.C. 112, first paragraph rejections and may result in the instant application receiving a final rejection.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee (WO92/00382). Lee makes the direct suggestion to use GDF-1 for rescuing neurons following axonal injury or in disease states leading to neuronal degeneration (page 14), rendering claims 1-3 *prima facie* obvious. The grounds of this rejection could be obviated by amending the claims to recite a method of promoting neuronal fiber outgrowth or neuronal survival by administering a therapeutically effective amount of both GDF-1 (SEQ ID NO:2) and NT-3, or, a method of promoting neuronal fiber outgrowth or neuronal survival of cerebellar granule cells by administering a therapeutically effective amount of GDF-1 (SEQ ID NO:2) to a patient in need of neuronal fiber outgrowth or neuronal survival of cerebellar granule cells.

11. No claim is allowed.

As allowable subject matter has been indicated, applicant's reply must either comply with all formal requirements or specifically traverse each requirement not complied with. See 37 CFR 1.111(b) and MPEP § 707.07(a).

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen Gucker whose telephone number is (703) 308-6571. The examiner can normally be reached on Monday to Friday from 0930 to 1800.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is currently (703) 308-4242, but Applicant should confirm this by phoning the Examiner before faxing.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

SG

Stephen Gucker

1/10/04